Recurrent variations in DNA methylation in human pluripotent stem cells and their differentiated derivatives.

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Public Summary:
We report the most comprehensive study of human pluripotent stem cell variation to date. We identified recurrent aberrations in X chromosome inactivation and imprinting that were maintained during differentiation. DNA hypomethylation was the most discriminate epigenetic feature of any tissue and was recapitulated by DNA demethylation during in vitro directed differentiation.

Scientific Abstract:
Human pluripotent stem cells (hPSCs) are potential sources of cells for modeling disease and development, drug discovery, and regenerative medicine. However, it is important to identify factors that may impact the utility of hPSCs for these applications. In an unbiased analysis of 205 hPSC and 130 somatic samples, we identified hPSC-specific epigenetic and transcriptional aberrations in genes subject to X chromosome inactivation (XCI) and genomic imprinting, which were not corrected during directed differentiation. We also found that specific tissue types were distinguished by unique patterns of DNA hypomethylation, which were recapitulated by DNA demethylation during in vitro directed differentiation. Our results suggest that verification of baseline epigenetic status is critical for hPSC-based disease models in which the observed phenotype depends on proper XCI or imprinting and that tissue-specific DNA methylation patterns can be accurately modeled during directed differentiation of hPSCs, even in the presence of variations in XCI or imprinting.